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Filed: January 22, 2002
RESPONSE TO OFFICE ACTION

Remarks

Rejection Under 35 U.S.C. § 103

Claims 16-21 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent Application Publication No. 2001/0018072 to Unger ("Unger") or U.S. Patent No. 6,565,885 to Tarara *et al.* ("Tarara"). Applicants respectfully traverse this rejection.

a. U.S. Patent Application Publication No. 2001/0018072 to Unger ("Unger")

Unger describes a solid porous matrix containing a surfactant and a bioactive agent. In one embodiment, the matrix is formed by spray drying a solvent, surfactant, therapeutic agent, and blowing agent (para. 0076). The therapeutic agent is not dissolved in the solvent, as required by the claims, rather it is suspended since it is "only marginally soluble in the solvent." (para. 0075). The only blowing agent disclosed by Unger is a liquid blowing agent, methylene chloride, which is not a volatile solid (*see* para. 0022). Unger does not disclose or suggest using a volatile solid pore-forming agent. One of ordinary skill in the art would not be motivated to modify Unger to arrive at the claimed methods. Therefore claims 16-21 are not obvious in view of Unger.

The Examiner's reference to U.S. Patent No. 5,976,574 to Gordon is unclear. Gordon is not cited by the Examiner in the current Office Action. Therefore, the issue of what Gordon does or does not disclose is irrelevant. Further, as noted by the Examiner, Gordon does not disclose or suggest a step of combining at least one volatile solid pore forming agent with a drug

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solution (Page 2 of the office action, Item No. 2). Therefore, even if Unger was combined with Gordon, claims 16-21 would not be obvious to one of ordinary skill in the art.

b. U.S. Patent No. 6,565,885 to Tarara et al. ("Tarara")

Tarara issued as a patent on May 20, 2003. Tarara's earliest claimed priority date is to provisional application, U.S.S.N. 60/060,337, filed September 29, 1997. The present application was filed on November 3, 2000 and claims priority to an application filed on May 27, 1999. Thus, Tarara was clearly published after the priority date of the present application, and could only be prior art under 35 U.S.C. §102(e). Assuming that the Examiner rejected the claims for obviousness based on a determination that Tarara is prior art under 35 U.S.C. §102(e), this rejection is respectfully traversed.

Legal Standard under 35 U.S.C. § 102(e)

35 U.S.C. §102(e) prior art includes patents "granted on an application for patent by another filed in the United States *before the invention by the applicant* for patent" 35 U.S.C. §102 (e) (emphasis added). A declaration under 37 C.F.R. § 1.131 may be used to "establish invention of the subject matter of the rejected claims prior to the effective date of the reference [...] on which the rejection is based." 37 C.F.R. § 1.131 (a). The declaration must show either (1) reduction to practice of the invention prior to the effective date of the reference or (2) conception of the invention prior to the effective date, coupled with due diligence from the effective date until a subsequent reduction to practice or the filing of the application. Chisum on Patents §3.08[1]. When a reference shows only part of the invention, such as a species within a

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generic invention, a Rule 131 affidavit is sufficient if it shows that the affiant had prior possession of that part of the invention disclosed by the reference. Chisum on Patents §3.08[1][b]. *In re Stempel*, 241 F.2d 755, 113 U.S.P.Q. 77 (C.C.P.A. 1957), the leading case on prior possession of part of an invention, explained that a reference "is valid only for what it discloses [therefore] if the application establishes priority with respect to that disclosure, and there is no statutory bar [the reference] is of no effect at all." 241 F.2d at 759-60. Therefore, a declaration under 37 C.F.R. § 1.131 is only required to antedate what is disclosed by the reference.

Tarara Is Not Available as Prior Art Under 35 U.S.C. 102(e)

Tarara claims priority to a provisional application filed on September 29, 1997. Tarara discloses using a spray drying feedstock which contains a bioactive agent, surfactant, and a blowing agent, optionally with an excipient (abstract; col. 17, lines 11-16). Some of Tarara's preferred embodiments also contain synthetic or natural polymers (see col. 11, line 63 to col. 12, line 16).

Enclosed is a declaration under 37 C.F.R. § 1.131 Julie Straub and Howard Bernstein. In their declaration, Julie Straub and Howard Bernstein state that prior to September 29, 1997, the earliest claimed priority date for Tarara, they conceived of and reduced to practice compositions that are formed by spray drying a feedstock containing a bioactive agent, a surfactant and a blowing agent. A declaration containing the same statements and data as the statements and data in the enclosed declaration was previously filed in related application, U.S.S.N. 09/706,045,

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which issued as U.S. Patent No. 6,932,983 on August 23, 2005, to overcome a similar rejection over Tarara.

As noted in the copies of the laboratory notebook pages attached to the Declaration (Exhibit A), microparticles containing air as the diagnostic agent were formed by spray drying (see page 14). Air bubbles were encapsulated in synthetic polymer microparticles by a spray drying process. The feed stock to the spray drying apparatus included a blowing agent (ammonium acetate), a surfactant (lecithin), polymers (poly(ethylene glycol)-co-poly(lactide-co-glycolide) (75:25) and D,L-poly(lactide)), and a diagnostic agent (air). This composition was homogenized to form an emulsion, which was then spray dried using a small-scale lab spray dryer. The resulting microparticles were echogenic (see page 105, injection 7).

Tarara defines "blowing agent" as "any volatile substance, which can be incorporated into the feed solution for the purpose of producing a perforated foam-like structure in the resulting dry microspheres." (col. 19, lines 26-29). Tarara specifically lists "[d]issolved or dispersed salts or organic substances which can be removed under reduced pressure by sublimation in a post-production step, such as ammonium salts, camphor, etc." (col. 19, lines 52-55). Thus ammonium acetate is a representative species of the genus of blowing agents disclosed in Tarara.

Tarara defines "bioactive agent" as "a substance which is used in connection with an application that is therapeutic or diagnostic in nature." (col. 6, lines 30-32). Tarara explains that "those skilled in the art will appreciate that any therapeutic or diagnostic agent may be

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incorporated in the stabilized dispersions.” (col. 6, lines 35-37) Air is a gas used in echogenic particles for ultrasound imaging techniques (*see e.g.* Appendix A, page 105, injection 7). Thus, air is a representative species of the genus of bioactive agents disclosed in Tarara.

Tarara defines “surfactants” as “any compound or composition that aids in the formation of perforated microparticles or provides enhanced suspension stability, improved powder dispersibility or decreased particle aggregation.” (col. 10, lines 14-18) Tarara specifically mentions lecithin as a typical surfactant (*see* col. 31, line 57). Thus, lecithin is a representative species of the genus of surfactants disclosed in Tarara.

As shown by the attached declaration and copies of pages from the inventor’s laboratory notebook, prior to September 29, 1997, applicants had conceived of and reduced to practice forming particles by spray drying a feedstock which contains a bioactive agent, surfactant, and blowing agent. Therefore, Tarara is not available as prior art under 35 U.S.C. § 102(e), and claims 16-21 are not obvious in view of Tarara.

Tarara’s earliest priority date for the relevant disclosure is September 29, 1998

The Examiner’s attention is directed to the fact that the earliest disclosure of including a volatile salt in the feed stock to the spray dryer is September 28, 1998, the filing date of PCT/US98/20602. The first three applications to which Tarara claims priority, do not disclose using volatile salts as the blowing or inflating agent. WO 99/16419, filed as PCT/US98/20602 on September 29, 1998, is the first priority application that lists a volatile salt as a suitable blowing agent. At page 17, lines 8-9 and page 20, lines 29-30, WO 99/16419 states that

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ammonium carbonate and camphor are suitable blowing agents. Therefore, Tarara's earliest priority date for the disclosure of including a volatile salt in the spray dried composition, as required by the pending claims, should be September 29, 1998. However, regardless of the priority date accorded Tarara, the enclosed declaration establishes that the applicants conceived of and reduced to practice compositions that are formed by spray drying a diagnostic agent with a surfactant and a blowing agent prior to the earliest priority date of Tarara.

Allowance of claims 16-21 is respectfully solicited.

Respectfully submitted,


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